Nitric Oxide in the Regulation of Intraocular Pressure

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Nitric oxide (NO), a gaseous transmitter, is formed in the tissues from L-arginine by NO synthase enzymes. NO activates soluble guanylate cyclase, which synthesizes cyclic GMP (cGMP). Many effects of NO are mediated by cGMP, and one of the major functions of cGMP is the relaxation of vascular smooth muscle. NO mediates both physiological and pathophysiological processes in the eye. NO may also regulate the intraocular pressure (IOP) acting at various sites in the eye such as ciliary body and trabecular meshwork. NO has been suggested to have a role either in the production of aqueous humor or in its outflow or in both. More likely NO is involved in the relaxation of ciliary muscle, which may lead to decreased resistance in the aqueous humor outflow mechanism. We and others have shown that topically administered NO donors lower the IOP in rabbits. Similarly, a cGMP analog lowered IOP in rabbits, which further indicated a central role of cGMP in the process. Study using intracameral administration of NO donors and a cGMP analog in rabbits indicated that the aqueous humor outflow increased. NO donors such as organic nitrates have also been suggested to influence the IOP in humans. However, we were not able to influence IOP or aqueous humor outflow in healthy volunteers with a single oral dose of isosorbide-5-mononitrate. In primary open-angle glaucoma decreased NO production has been reported. The effects of NO on retinal cells seem to be biphasic, low concentrations protective, high concentrations toxic. Pharmaceutical industry has developed NO donating compounds from old antiglaucoma drugs or novel compounds with NO donating properties or molecules directly increasing the cGMP levels.

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